# THE PREPARATION AND REACTIONS OF PARACHLOROPHENYLARSINE

BY

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I HEREBY RECOMMEND THAT THE THESIS PREPARED UNDER MY

SUPERVISION BY Wallace H. Carothers

ENTITLED The Preparation and Reactions of p-Chlorophenylarsine

BE ACCEPTED AS FULFILLING THIS PART OF THE REQUIREMENTS FOR

THE DEGREE OF Master of Science

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# THE PREPARATION AND REACTIONS OF PARACHLOROPHENYLARSINE.

## I. THEORETICAL AND HISTORICAL.

Arsenic occurs in the periodic table in the fifth vertical column below phosphorous which stands just under nitrogen, a fact which would lead to the prediction that arsenic and nitrogen would show some similarities. Physically they are, of course, quite different, but chemically their properties bear out this prediction in many respects. Thus, both elements form stable hydrides in which the element is trivalent; both form stable oxides in which the element is either tri- or pentavalent; both form halides [1, 2].

Similar analogies exist in the formation of organic derivatives and in the chemical properties of these derivatives. The hydrides of both elements yield derivatives in which one hydrogen is replaced by an alkyl or aryl group, the primary amines being thus derived from ammonia, and the primary organic arsines from arsine. Amines were predicted to be capable of existence by Liebig in 1842 [3], were first prepared by Wurtz [4], and since then have been extensively studied and have been found to be of enormous importance in organic chemistry, the aromatic amine compounds being especially important in the synthesis of other compounds of many diverse types.

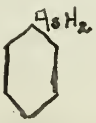
The existence of primary organic arsines would of course, be predicted by analogy, but attempts to prepare compounds of this type[5] failed until A. W. Palmer succeeded in reducing methyl and

[1] Wm. H. Dehn Amer. Chem. Journ. 33, 101 (1905)
[2] Gilbert T. Morgan, Organic compounds of Arsenic and antimony, xi.
[3] Handworterbuch, 1, 689.
[4] Ann. Cham. (Liebig) 71, 330, 76, 318.
[5] Ann. Chem., 107, 285.

phenyl arsonic acids and isolating the corresponding arsines.[6] It then appeared that the failure of previous investigators had been due to the absence of precautions to protect the product from the air; primary arsines being oxidized instantaneously. Since then several other primary arsines, both aromatic and aliphatic have been prepared[7], and there is no apparent theoretical reason why the list should not be extended indefinitely.

The properties of primary arsines have been studied most extensively by Dehn [8]. He found that like the primary amines they react readily with alkyl halides with the formation of secondary and tertiary arsines and quarternary arsonium compounds, that they are formed by the reduction in acid solution of any monoarylated or monoalkylated arsenic compound, that in certain cases they combine with sulphuric acid with the formation of unstable salts. On the other hand the primary arsines are oxidized much more readily than are the amines, halogens readily replace the hydrogen attached to the arsenic, etc., showing the effect of the more positive character of the arsenic atom.

Phenyl arsine is the structural analogue of aniline, and as may be seen from a comparison of the formulas of the two compounds the formal resemblance is very close, especially when the proximity of nitrogen and arsenic in the periodic table is taken into consideration.

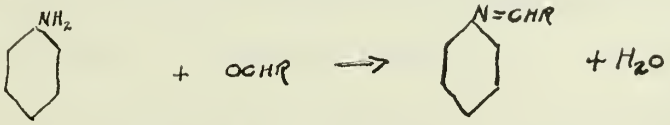


[6] Ber. d. Chem. Ges. 34, 3594.

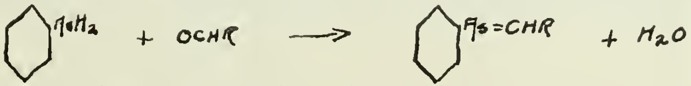
[7] Ber. (1901) 34, 3594.
Amer. Chem. Journ. (1908) 40, 113.
D. R. P. 269, 843; 269, 744, 251, 571; 275, 216;
Chem. Abs. 11, 3256.

[8] Am. Chem. Journ., 33, 101; 40, 88; 35, 1 (1906)

To what extent this structural analogy finds its outward expression in chemical properties has been indicated above for certain reactions. But there are other reactions in which these similarities might be expected to manifest themselves. Thus, aniline condenses with certain aldehydes according to the following scheme[9]:



Phenyl arsine might be predicted to react in a similar manner:



This reaction has been studied by Adams and Palmer[10] who found that no reaction takes place until a drop of Hcl is added. A vigorous reaction then sets in. The reaction instead of following the above course, went as follows:

The product is thus a new type of organic arsenic compound. This result is of considerable importance for two reasons. In the first place, the existence of such a type is of theoretical interest; in the second place, the most promising field for researches in which the purpose to discover superior compounds to replace arsphenamine and neo-arsphenamine, is in the study of new types of organic arsenic compounds[11]. Old types have been pretty carefully studied, and the chief objection to those which have so far proved most successful in the treatment of syphilis and virulent skin diseases is instability, a defect which seems to be inherent in the type (the arseno grouping) and which is fatally retained thru

[9] Vide L. Rugheimer, Ber. d. Chem. Ges., 39, 1653 (1906)

[10] Journ. Am. Chem. Soc., 42, 2375 (1920). The structure of these compounds has never been definitely proved.

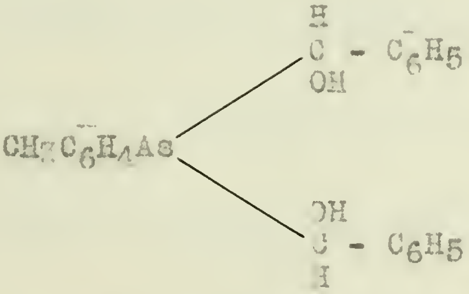
[11] Vide ibid.

all the enormous series of derivatives of this type which have been studied.

The purpose of the present investigation was to study the properties of certain analogues of phenyl arsine and their reactions, especially the reaction with aldehydes. The character of the reaction product between primary amines and aldehydes depends upon the character of the aldehyde, and also upon the nature of the substituent in the ring of the amino compound.[9] It should be of interest to determine if similar effects are operative in the case of the arsines.

| | % arsenic |
|---|---|
| Calculated for $CH_3C_6H_4AsH_2(C_6H_5CHO)_2$ | 19.71 |
| .1507 gram of substance reduced 8.03 c.c. of iodine solution (1 c.c.=.003515 g. arsenic) | 18.73 |
| .1391 gram of substance reduced 7.45 c.c. of iodine solution | 18.82 |

The above product evidently was a condensation of one mole of o-tolylarsine and two moles of benzaldehyde. The following formula:



is a possible and probable one. This condensation product is hydrolyzed by cold, concentrated, hydrochloric acid and slightly by boiling dilute hydrochloric. It is not hydrolyzed by boiling five minutes with 30% sodium hydroxide solution.

## o-Tolyl Arsine and Paraldehyde.

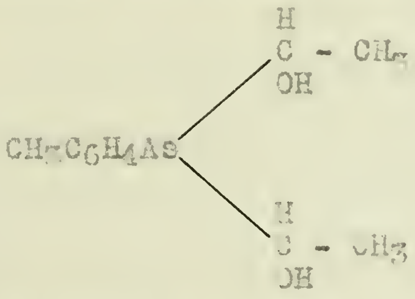
A similar experiment was carried out to determine the action of paraldehyde on o-tolylarsine. To about 25 grams of the arsine a few drops of concentrated hydrochloric acid and about 35 grams of paraldehyde were added. The mixture became slightly warm but not so warm as in the previous experiment. When the reaction had ceased, the flask was sealed and set aside. After a few days the mixture contained a white solid and was rather turbid. The excess paraldehyde, about 18 grams, was distilled off at 180 mm pressure, leaving a clear yellow solution. An attempt was made to distill this at the same pressure, but it decomposed, turning red. At 23 mm. it boiled at 165°. On second distillation, about 18 grams of product, slightly

turbid, was obtained. In neither case was all of the product distilled, as it charred slightly on getting to a low volume. On standing a few days a white solid settled out. The liquid was decanted from the solid and on distillation, a clear product, boiling at 165°,21mm., was obtained. The index of refraction is

$(n)^{30}$ 1.5573

| | % arsenic |
|---|---|
| Calculated for $CH_3C_6H_4AsH_2(CH_3CHO)_2$ | 29.25 |
| .0974 gram substance reduced 7.67 c.c. of iodine solution (1c.c.=.003528 gram arsenic) | 27.78 |
| .1527 gram substance reduced 12.04 c.c. of iodine solution | 27.82 |

This substance possibly has the structure:



similar to the one suggested for the condensation product of benzaldehyde and o-tolylarsine.

The paraldehyde condensation product mentioned above was hydrolyzed by cold, concentrated hydrochloric acid, giving a strong odor of paraldehyde and yellow and red solids. These likely were oxidation products of the o-tolylarsine which was formed by the hydrolysis. Boiling dilute hydrochloric hydrolyzes the condensation product slightly. It is not hydrolyzed with boiling dilute or cold 30% alkali, but on boiling with 30% sodium hydroxide, it is hydrolysed.

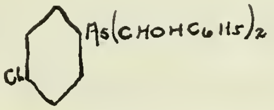
## II. DESCRIPTIVE

p-Chlorophenylarsine does not appear in the literature. For the present investigation it was prepared by a method similar to that described in D. R. P. 251,571 [12]. Its preparation and properties are described in detail in the experimental part of this paper.

The condensation of p-chlorophenylarsine with benzaldehyde was carried out as follows[13]: To one mole of the pure redistilled arsine a little over two moles of the aldehyde were added, then a few drops of conc. HCl solution. The mixture immediately became hot, and completely solidified within a half an hour to a white, amorphous solid. The reaction mixture was, of course, kept in an atmosphere of $CO_2$. On standing for an hour in an atmosphere of $CO_2$, the mass gradually began to turn yellow and at the end of three or four hours it was found to have changed completely to a canary yellow. This material was partially soluble in hot chlorobenzene. It was extracted with hot chlorobenzene, and the hot extract filtered. On cooling the filtrate, long silky needles separated which gradually aggregated to cottony masses which seemed to render the solution almost a solid mass. These crystals, on filtering off the liquid were found to be very light, the yield from 20 grams of the arsine never amounting to over three grams and often falling below 0.5 gram. They were recrystallized several times from a mixture of chlorobenzene and alcohol. The results were the same when dry, gaseous instead of aqueous HCl was used as a catalyst.

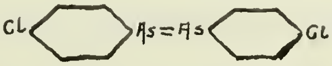
[12] Friedlander XI, 1024.
[13] Vide Adams and Palmer ibid.

The product thus obtained was an extremely light, cottony mass, melting at 218-218°." C. (corr.) (211.0-211°.2, unc.) and gradually changing to a hard, brown, caramel-like mass when heated for some time below its melting point (e. g. at 140°). It was insoluble in water, dilute acids or alkalies, slightly soluble in alcohol, ether, benzene, and ligroin, and very soluble in chlorobenzene. It thus resembled quite closely in all its physical properties the analogous compound of phenyl arsine and benzaldehyde obtained by Adams and Palmer. The analytical data, however, did not bear out this conclusion very closely. If this substances has the formula



it is evident that its formation does not represent the chief product when ultimate and most stable conditions of equilibrium have been reached. In all cases the chlorobenzene insoluble residue constituted at least 95% of the reaction product, and apparently the relative proportion of the latter product increased as the reaction mixture was allowed to stand before extraction with chlorobenzene. This residue was at first a bright yellow, sticky mass, smelling strongly of benzaldehyde. On standing in the air it gradually became lighter in color and dry. After a couple of weeks it was found to be mostly soluble in hot 10% NaOH solution although a dirty, sticky residue remained insoluble. On dilution, this solution became turbid, but no precipitate appeared until the solution was made acid with HCl. The precipitate thus formed was light yellow-grey, and of the consistency of molasses. On standing for some time, it gradually became solid and granular. This

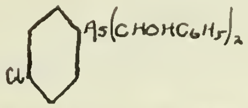
precipitate was filtered off and dissolved up in 95% alcohol, almost completely covered and allowed to evaporate very slowly. After three weeks it was found that the amorphous yellow mass which remained contained may clusters of tiny, needle-like crystals. These were isolated and identified as p-chlorophenylarsonic acid. The inference was that the main product of the reaction was not the condensation product expected, but p-dichloroarsenobenzene:



This accounts for the changes above mentioned, for the arseno compounds are usually yellow, and they are all oxidized slowly by the air to arsonic acids. Attempts to isolate the arseno compound failed, as would be expected because these compounds are difficultly soluble in most reagents, and usually amorphous, and some benzaldehyde was present to complicate matters.

It was also attempted to condense p-chlorophenylarsine with paraldehyde. The reaction was carried out in the same way as with benzaldehyde. On the addition of HCl, the mixture became warm, but remained liquid. After standing for 12 hours it was dissolved in benzene, dried with fused calcium chloride, filtered, and fractionated under diminished pressure. Most of the condensation product was found to distill over, but at the end decomposition took place rather suddenly, leaving in the flask a red, sticky mass. The distilled product thus obtained was a colorless liquid boiling at 183° under 23 mm. of mercury. It was redistilled. The yield in this case was much better, amounting to about 30% of theory. The product had a refractive index of 1.5728 at 25°, and a specific gravity of .7481. It was insoluble in water and dilute

HCl, but soluble in benzene and chlorobenzene. Analysis indicated the formula $C_{10}H_{14}O_2AsCl$ which corresponds to



This compound was very unstable. On standing it gradually underwent change with the separation of a solid white material. The nature of this product was not determined, the amount obtained being insufficient for analysis. It was insoluble in 20% NaOH, even after standing for a long time in the air, and hence could scarcely have represented an oxidation product of the arsine. It was soluble in chlorobenzene and upon evaporating off the solvent under diminished pressure at ordinary temperatures, no solid separated out, but a viscous liquid remained very like the material from which it originally separated.

This investigation was extended to a study of the properties of certain other arsines. The preparation of p-aminophenylarsine is described in D. R. P. 251,571[14]. For the present investigation it was prepared by the same method as that used in the preparation of p-chlorophenylarsine. The pure aminophenylarsine was also isolated and condensed in the same way using three moles of benzaldehyde instead of two. It was supposed that the amino group would first condense in the absence of HCl, and that the arsine would then react upon the addition of HCl. This prediction was borne out by the general behavior of the mixture. On adding the benzaldehyde the mixture became quite warm, and after cooling, when a few drops of conc. HCl had been added, the mixture heated up again. The reaction mixture now gradually solidified to a trans-

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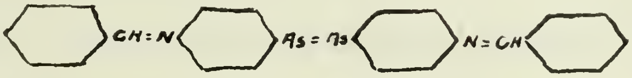
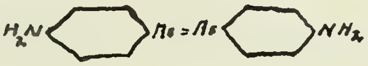
[14] Friedlander XI, 1024.

lucent, almost colorless mass. It was kept in an atmosphere of $CO_2$ throughout. After standing in carbon dioxide for twelve hours it was found that red spots had appeared and, upon exposing the mass to the air, the red color gradually spread throughout the whole mass. Benzaldehyde was regenerated. The mass now was found to be soluble in chlorobenzene, from which solution it was precipitated by the addition of dilute aqueous HCl. After filtering and drying, a rather heterogeneous and very hard reddish mass remained which was apparently completely insoluble in any common organic solvents. It was suspected of being:



Since the compound

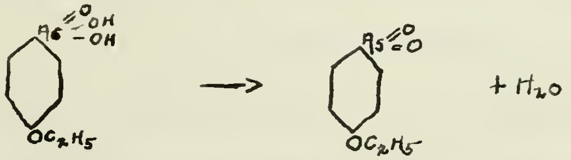


resembles it in color and general solubility behavior[15]. An attempt to hydrolyze the compound with dilute HCl and thus to obtain p-diaminoarsenobenzene resulted in a decomposition of the molecule with the formation of black tarry material. Analysis of the reddish material showed 22.26% arsenic. The theoretical value for a compound of formula I is 29.38%. The disparity is probably due to the impurity of the material. Its hard, non-crystalline character and insolubility made it impossible to purify.

p-Phenetylarsine was prepared in the same way as p-chloro- and p-aminophenylarsine. Apparently it underwent very considerable decomposition either during the reduction or during distillation, for the product showed 14.04% of arsenic instead of the theoretical value of 37.75%. It smelled strongly of phenetole. About half of

[15] D. R. P. 206,057

a gram of the arsine was therefore exposed to the air. A white precipitate formed at once, and after standing for several hours an oil still remained. This was separated by extracting the solid material with a little ether, filtering, and pulling off the ether from the filtrate at ordinary temperatures under diminished pressure. The residual oil amounting to about 0.5 g. was identified as phenetole by its odor and boiling point. The residual white solid amounting to about 0.2 g. was analyzed after drying at 80° for two hours. It showed 31.60% of arsenic. The theoretical value for p-phenetylarsonic acid is 30.49% and for the corresponding arsine oxide, 35.38%. The white powder was therefore chiefly phenetylarsonic acid, containing some phenetylarsine oxide as an impurity. It melted at 174-6° in a capillary in an oil bath in which the temperature was rapidly rising. If, however, the temperature rose slowly, especially within 10° of this melting point, it did not melt under 275°. If a sample of the material was melted and frozen repeatedly it became infusible. This behavior is characteristic of the aryl arsonic acids[16], and is due to the loss of a molecule of water.



According to Bertheim,[17] p-phenetylarsonic acid melts at 209-10°. The observed melting point is of course of no special significance except to indicate that the sample was not pure p-phenetylarsonic acid, a conclusion which is borne out by the results of the analysis.

The product obtained by the reduction of p-phenetylarsonic

[16] Morgan, Organic Compounds of Arsenic and Antimony, p. 74
[17] Ber. (1908) 41, 1854

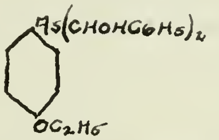
acid thus undoubtedly consisted of p-phenetylarsine mixed with phenetole, the latter being fromed by some secondary reaction taking place during the reduction or the steam distillation, and involving the splitting off of arsinic from the ring.

The boiling point of the highest boiling fraction of the mixture was 162-5° under 18 mm. and this undoubtedly represents the boiling point of pure phenetylarsine. A rather remarkable fact about this mixture is that on oxidation it immediately yields a white powder. Now the arseno compound represents the first possible stage in the oxidation of an arsine, and p-diethoxyarsenobenzene is known to be yellow.[18] Apparently the arseno compound either was not intermediate, or it was under these conditions oxidized more rapidly than it was formed. This behavior is rather unusual, and combined with the lability of the $AsH_2$ group in phenetylarsine, indicates the remarkable and unexpected influence which the $OC_2H_5$ group has on the properties of the phenylarsine rest.

The mixture of phenetylarsine and phenetole was condensed with benzaldehyde as follows: To 14 g. of the mixture, 16 g. of benzaldehyde was added (2 moles assuming that the phenetylarsine is 100% pure) and then a few drops ofaqueous HCl. Heat was evolved, and after standing for 12 hours in an atmosphere of $CO_2$ it was observed that crystals had separated. Without admitting any trace of air, the mixture was now steam distilled until nothing further was carried over. About two grams of a yellow, sticky solid remained in the distilling flask, while in the receiver a considerable quantity of yellow oil had collected under the water. It was

[18] Michaelis., Ann., 320, 300 (1902)

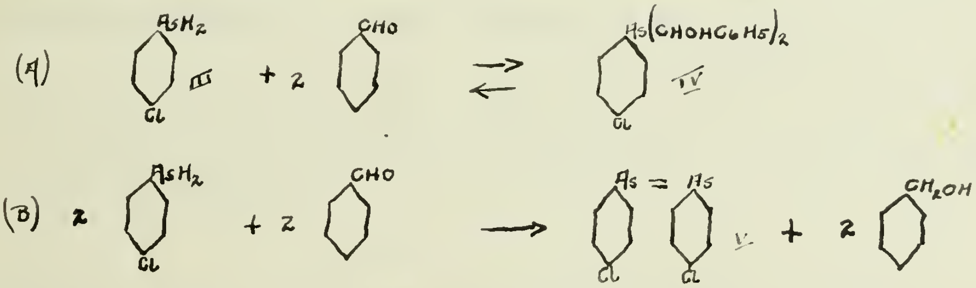
separated off and exposed to the air. Benzaldehyde and phenetole were obviously present, and later some crystals separated which proved to be phenetylarsonic acid. Now phenetylarsonic acid is not volatile, nor are any of the other possible oxidation products of phenetylarsine. It was, therefore, necessary to conclude that the arsine itself had distilled over. Some of the arsine must, therefore, have remained unchanged in spite of the fact that the benzaldehyde was present in large excess, or the arsine must have been regenerated from its combination during the distillation. The residue from the steam distillation was now examined. It was found to be soluble in chlorobenzene, and ethyl alcohol, from which solution on cooling there separated long, silky needles, which were supposed to be the condensation product:



After recrystallization and drying they melted at 220-223° (corr). This product amounted to less than 0.1 g., and an attempt to determine the arsenic content did not yield a result of any significance. The filtrates from both crystallizations were combined and the solvent evaporated off at ordinary temperatures. The residue remaining was a sticky viscous, yellow liquid. It amounted to about 1.5 g. It was supposed to contain some arseno compound, and some benzaldehyde which had been mechanically held back during the distillation.

## III. SIGNIFICANCE OF RESULTS.

It is evident that the reactions of these arsines with benzaldehyde are very complex, and that in any case, when equilibrium is reached, the product of the type RAs $(CHOHC_6H_5)_2$ represents but a small fraction of the products formed. It is possible to explain the phenomena observed on the addition of p-chlorophenyl arsine to benzaldehyde by the reactions indicated below.



The reaction goes practically quantitatively at first to the formation of IV which is a white solid. At the same time reaction B sets in, but is much slower than A. However, it is more complete, so that ultimately most of the arsine present is changed into V. This theory is borne out by several facts, the most important of which is the color change above mentioned. Benzyl alchol was never isolated from the reaction mixture, but Mr. C. S. Palmer of this laboratory has identified it as one of the products in the reaction between phenylarsine and benzaldehyde. In one case alcohol was added to the arsine before the addition of benzaldehyde. Heating and the formation of a solid took place as usual on the addition of benzaldyhyde, but neither reaction A nor B could have been complete; since most of the arsine was unchanged at the end of an hour and on exposing the mixture to the air, much heat was evolved, and p-dichloroarsenobenzene formed.

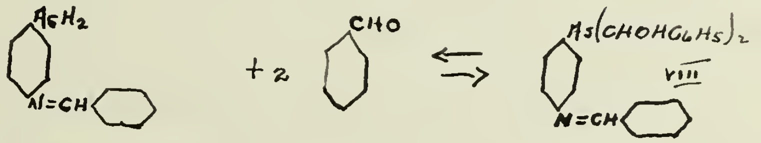
The reversibility of reaction A must be questioned. Products

of the type IV are fairly stable although, at least in certain cases, they decompose much below their melting points, this decomposition being almost complete in two hours at 140° in the case of the product IV.

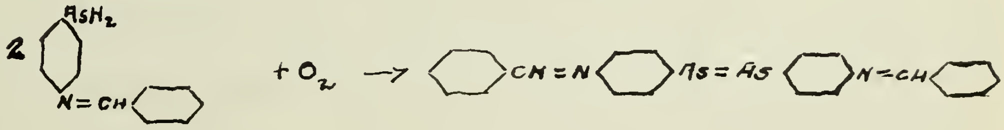
The behaviour of the other two arsines studied furnished certain additional evidence. Thus, in the case of p-aminophenylarsine care was taken to add just exactly the theoretical amount (3moles) of benzaldehyde. All the benzaldehyde disappeared after the addition of the HCl, but on exposing to the air, it was at least partially regenerated. The most rational explanation of this behaviour necessitates the assumption of a reversible reaction similar to the above:

(C)

(D)

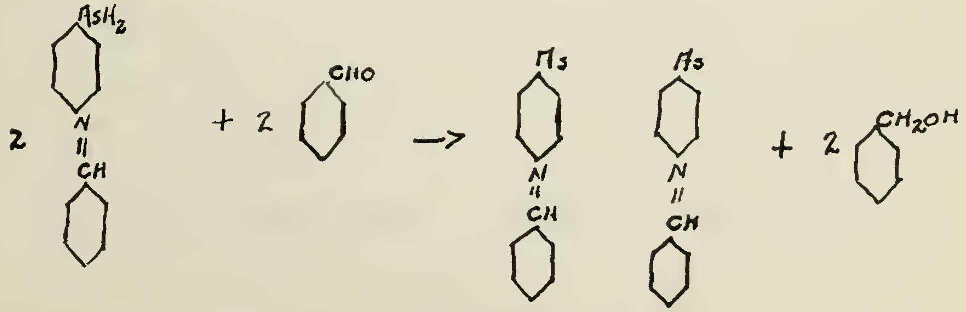


(E)



The reaction

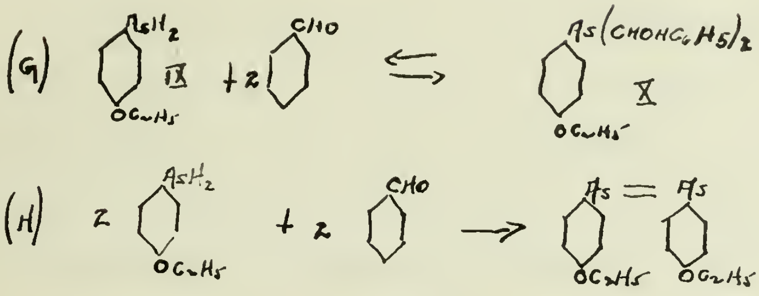
(F)



is less in evidence here, since in the course of 12 hours only a few reddish spots had appeared in the mixture in the absence of air; but these were sufficiently obvious to justify the assumption

that some aldehyde had been reduced, providing F is the proper explanation for the formation of the reddish product.

Similar explanations suffice to account for the observations made in the case of p-phenetylarsine



In this case also reaction H was not so much in evidence, but that it actually took place to some extent is indicated by the yellow color of the product obtained after the completion of the steam distillation. That is to say, reaction H was very slow, just as was reaction F; but that reaction G was reversible was indicated by the fact that most of the arsine originally present appeared in the distillate from the steam distillation, in spite of the fact that a large excess of benzaldehyde was present.

Thus it is concluded that compounds of the type IV, VIII and X were formed, but that the reaction by which they formed was in each case reversible so that they were each in equilibrium with the arsine from which they are derived. In each case the equilibrium was displaced by the removal of the arsine from the field of the reaction: the p-chlorophenylarsine was oxidized by the benzaldehyde to the corresponding arseno compound; the p-aminophenylarsine was oxidized on exposure to the air to the arseno compound; the p-phenetylarsine was removed by the steam.

The chief objection to this explanation is that there is no direct evidence for the evolution of arsine from these condensation products, and while it is pointed out that those compounds with which this study is concerned showed no very high degree of stability, and in certain cases (notably the compound of paraldehyde with p-chlorophenylarsine) were decidedly unstable; yet it must be admitted that the above explanations cannot be regarded as completely consistent and satisfactory unless they are fortified with some additional assumptions, such as: that the reverse reaction is catalyzed by some substance which is absent after the purification, or that in some manner, the purified product is more stable than that from which it was derived. The basis of these speculations is made additionally insecure through the fact that the structore of these condensation products has never been definitely established.

## IV. EXPERIMENTAL PART.

1. Preparation and properties of p-chlorophenylarsonic acid: This substance has been prepared by Bertheim[18] from arsanilic acid by the Gattermann diazo reaction. For the present investigation it was prepared from p-chloroaniline by a modification of the Bart's reaction[19], the coupling being carried out in the absence of free alkali[20]. A typical run is described below:

126 g. of p-chloroaniline was stirred up by means of an efficient mechanical stirrer with 600 cc. $H_2O$ and 180 cc. conc. HCl (s. g. 1.19), cooled to 0°, and diazotized by the addition of 68 g. of sodium nitrate in 250 cc. of water, the temperature being kept below 7°. 350 g. of crude $As_2O_3$ (theoretical plus 80%) was dissolved in 1.5 liters of water to which 565 g. of sodium carbonate had been added by heating on the water bath for two hours with occasional shaking. Some of this material usually failed to go into solution. The mixture was, therefore, filtered with suction, and to the filtrate 10 g. of anhydrous copper sulphate was added with stirring. The solution was then cooled to approximately room temperature and the diazo solution siphoned into it very slowly. The solution was stirred constantly with a motor stirrer during this addition. A tendency to foam limits the speed of the addition of the diazo solution. It is, therefore, necessary to use as large a vessel as possible for this reaction, not smaller than 5 liters --- preferably much larger. Foaming can often be greatly mitigated by the addition of a few cc. of benzene occasionally. Stirring is

[18] Ber (1908) 41, 1854.
[19] D. R. P. 254, 092, Frdl., 11, 1030 (1913)
[20] J. Ind. Eng. Chem. 11, 825 (1919)

continued for four hours after the addition of the diazo solution is complete. The mixture is then allowed to stand for 12 hours and filtered with suction from the tar. The filtrate is clear and slightly greenish in color. It is made acid with glacial acetic. The addition of the acetic acid must be carried out very carefully, since the mixture may foam violently. If the approximate quantity of acid required is known, the solution may be added to the acid. The foaming under these conditions is much less[21]. The purpose of the addition of the acetic acid is to precipitate out the excess of $As_2O_3$, it having been found experimentally that arsenious acid is precipitated almost quantitatively[22] from solutions of its salts by the addition of acetic acid, while p-chlorophenylarsonic acid is not so precipitated. If the $As_2O_3$ thus precipitated is now filtered off, the filtrate will be found to be perfectly clear, and on the addition of conc. HCl (about one-fourth the total volume) the

21. J. Am. Chem. Soc. <u>43</u>, 181 (1912)

22. That is, for the purposes under consideration. The solubility of $As_2O_3$ in water approaches 20 g. per liter at ordinary temperatures. $HAsO_2$ is, however, ionized in 0.1N solution very slightly---between 0.002 and 0.008% according to A. A. Noyes, Qualitative Chemical Analysis, p. 123. Acetic acid in similar concentrations is ionized to the extent of 1½2%. Hence, in a solution of $As_2O_3$ containing acetic acid, the concentration of $AsO_2^-$ will be very low,---probably of the order of .0001 equivalents per liter (mass action effect). Any further repression of the ionization of $HAsO_2$ by an increase of the hydrogen ion concentration (addition of HCl) will, therefore, of necessity be extremely slight; and hence will have very little effect on the total concentration of $HAsO_2$. $H_3AsO_4$ is a much stronger acid than $HAsO_2$ (Ionization 20-45%) and p-chlorophenylarsonic acid would be predicted to be of the same order, and its solubility in water should be quite appreciable (cf. phenylarsonic acid). Acetic acid in the presence of large quantities of sodium acetate which are present does not furnish a sufficiently high concentration of hydrogen ions to exceed the solubility product of p-chlorophenylarsonic acid, but HCl does; and, moreover, the salting out effect of a moderately concentrated solution of HCl on the neutral molecules should be much greater than that of HCl on the neutral molecules of $HAsO_2$, a very weak electrolyte. See Washburn, Principles of Physical Chemistry 1915, pp. 227, 228.

p-chlorophenylarsonic acid will be precipitated as a perfectly white, granular precipitate. It is filtered off with suction, and thoroughly washed with cold water to remove any traces of salt, and dried for several days by exposure to the air. The product is a fine, white tasteless, dusty powder. The yield amounts to about 200 g. or 85% of theory. Its solubility behavior is indicated below:

| Solvent | Hot | Cold |
|---|---|---|
| Water | Somewhat | Sparingly |
| Dilute alkalies | Very soluble | Very soluble |
| Conc HCl | Very soluble | Insoluble |
| Alcohol | Very soluble | Sparingly |
| Ethyl acetate | Soluble | Somewhat soluble |
| Glacial acetic acid | Quite soluble | Soluble |
| Ether | Somewhat soluble | Somewhat soluble |

In a capillary tube a sample of the crude acid did not melt, but decomposed at about 320°. Similarly a sample recrystallized from alcohol decomposed at 348°. It crystallized in needles from alcohol, glacial, acetic, or hot concentrated HCl. The latter is an ideal solvent so far as solubility behavior is concerned, and moreover, boiling with HCl would probably distill off as $AsCl_3$ any traces of $As_2O_3$ which might be present; but analysis of samples recrystallized from this solvent always showed too high a chlorine content, howsoever thoroughly they were washed with boiling water. The sample used in obtaining the following analytical data was crystallized once from glacial acetic and twice from 95% ethyl alcohol and dried to constant weight at 90° under diminished pressure.

.1612 g. sample used 26.38 cc. $I_2$ sol. = 31.58% As
.1782 g. sample used 28.77 cc. $I_2$ sol. = 31.89%
.1966 g. sample used 31.60 cc. $I_2$ sol. = 31.74%
1 cc. $I_2$ sol = .001975 g. As Average 31.74%
.4190 g. sample gave .2539 g. AgCl = 14.99% Cl
.5190 g. sample gave .3176 g. AgCl = 15.14% Cl
Average = 15.06

Calculated for $C_6H_6O_3ClAs$: As, 31.71%; Cl, 15.01%.

The arsenic was determined by the method of Ewins[23] and the chlorine by the method of Carius.

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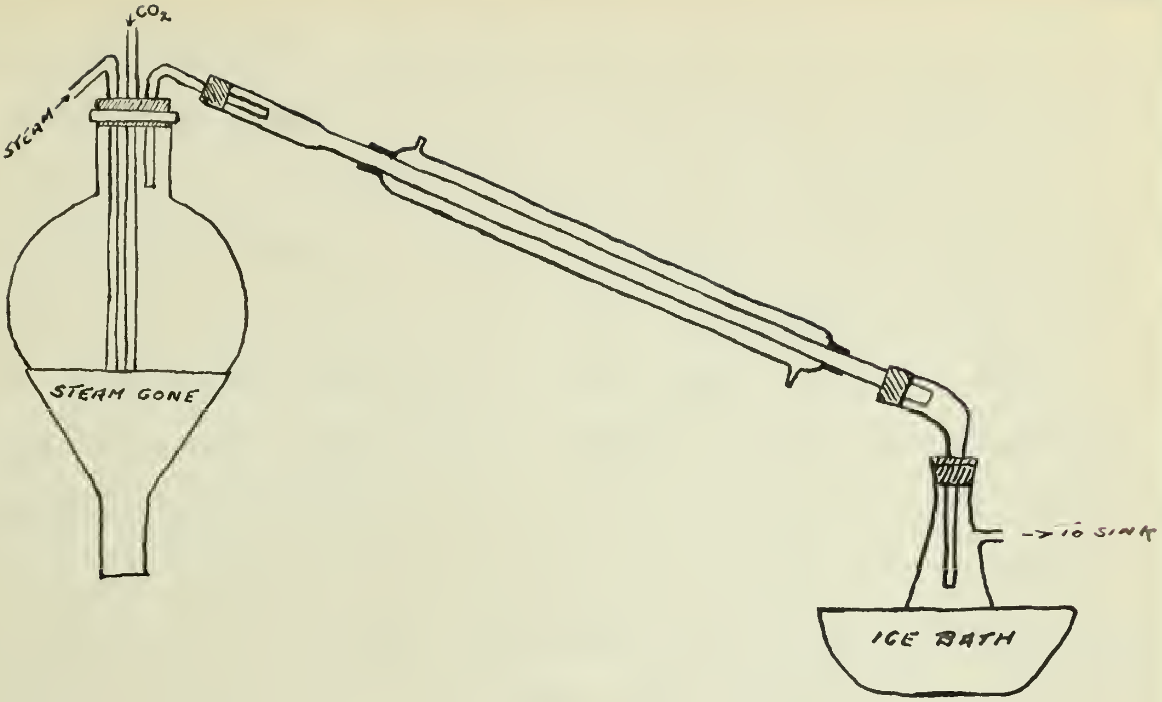
[23] Chem. Soc. Trans. (1916) 109, 1356.

2. Preparation and properties of p-chlorophenylarsine; Considerable difficulty was experienced in working out the proper conditions for the reduction of p-chlorophenylarsonic acid. The method finally adopted was as follows: 70 g. of p-chlorophenylarsonic acid and 350 g. of thoroughly amalgamated zinc dust were placed in a 3 liter round bottom flask, and 250 cc. of methyl alcohol added. The flask was provided with a two hole rubber stopper. Through one of these holes extended the lower end of a long glass condenser, the upper end being provided with a mercury trap consisting of a bent glass tube dipping into a tube of mercury. The other hole of the stopper carried a 3mm. glass tube about two decimeters long, and connected at the upper end with a 500 cc. dropping funnel. All joints were sealed with paraffin. The dropping funnel was filled with conc. HCl, the long tube filled with the acid and the stop-cock so regulated that the acid dropped in at the rate of about 3 or 4 drops to the minute. The combined effects of capillarity and the pressure inside the flask prevented the long tube from emptying even if the acid should all run out of the funnel during the night. About a liter of conc. HCl was thus added, and the run was considered complete when the zinc had all or practically all disappeared. This usually required from three days to one week. The stopper was now removed from the flask and quickly replaced by another bearing three glass tubes,---one connected to a source of steam, another to a source of $CO_2$, and another to a condenser. The whole set-up is illustrated in the following diagram:



Before admitting steam the apparatus was permitted to fill completely with $CO_2$. Steam was then passed through for about four hours. The arsine solidified from time to time in the condenser, and was pushed out by shutting off the condenser water and blowing out with $CO_2$. When the distillation was complete, the stopper bearing the adaptor was removed and immediately replaced by one bearing a right-angled tube attached to a source of $CO_2$. The suction flask was now removed from its ice bath. The p-chlorophenylarsine was found collected as dark solid at the bottom of the flask. A little glass wool was stuffed into the tubulure of the suction flask, the flask tipped, and the water pushed through the tubulure by the entrant steam of $CO_2$. The stopper was partially removed without, however, removing the end of the $CO_2$ tube and 200 cc. of ether added. The tubulure of the suction flask was inserted into the mouth of a 500 cc. separatory funnel filled with $CO_2$ and the etheral solution poured out. The flask was washed with a little ether and the process repeated. Water was drawn off from the bottom of the funnel

and then solid KOH and fused CaCl2 were added to the solution, and it was allowed to dry for two hours. The method of transferring the ethereal solution to the distilling flask was as follows: The Claissen flask was provided with a stopper bearing two tubes, one a capillary for $CO_2$ (as in a Brühl apparatus), and the other bent twice at right angles and closed at the lower end with a piece of stoppered gum tubing. Dry $CO_2$ was admitted through the capillary from mercury trap so arranged as to provide the gas at a constant pressure slightly greater than atmospheric. The Claissen flask was connected with a receiver consisting of an ordinary distilling bulb, and the latter with an air pump and a manometer as in an ordinary vacuum distillation. After the system had been alternately evacuated to the limits of the pump and filled four times with $CO_2$ at the pressure of the source, the stopper was pulled off from the right-angled tube and the latter dipped into the ethereal solution, $CO_2$ being continuously admitted. The $CO_2$ was then shut off and the suction turned on, and the flask filled with ether. The suction was so regulated as not to draw in any air, and as soon as the desired amount of ether was drawn in the suction was shut off and the $CO_2$ turned on. The separatory funnel was then withdrawn and stoppered, the right-angled tube closed, the ether pulled off in vacuo, and the process repeated until all the solution had been transferred to the flask. The solution was then fractionated. No special receiving flask was necessary, providing that the whole system was filled with $CO_2$ before changing receivers. Considerable experience taught that the best method of ensuring complete exclusion of air from the final product was as follows:

When distillation was complete, the suction was cut off and the system filled with $CO_2$ the stop-cock to the source being left open. When the rubber suction tube was now pulled from the glass delivery tube of the receiving flask, a stream of $CO_2$ rushed out of that tube and effectively prevented the ingress of any air. The rubber suction tube was then replaced by a rubber tube through which a stream of $CO_2$ poured, and the receiver drawn off from the delivery tube of the distilling flask. No air could enter the top of this flask because $CO_2$ was passing continuously out; and hence it was not necessary to stopper the flask until the $CO_2$ was cut off. This arrangement made it possible to draw out samples, etc. without any danger of contamination from the air. The optimum yield of twice redistilled product was about 26 g.

Several other methods for reducing the arsonic acid were tried without success. The presence of the methyl alcohol seems to be absolutely essential, probably because the solubility of the arsonic acid in water is not great. Some traces of arsine as indicated by the odor were always formed in reductions carried out without the use of methyl alcohol, but no arsine could be isolated. Attempted reductions using zinc dust and solid NaOH also failed. Ether extraction methods also were unsuccessful, supposedly because no considerable reduction took place unless methyl alcohol was present, and in its presence the ether extraction method is complicated by the considerable solubility of ether in the alcohol water mixture.

p-chlorophenylarsine which has been twice redistilled is a solid crystallizing in very thin, flat, perfectly transparent leaves. These crystals often attain a size of 1.5 cm. square, and in the reduction of the arsonic acid where some of the arsine vapor is carried

up out of the surface of the liquid, they condense against the sides of the flasks, standing out at right angles to its surface.

The odor is characteristic and persistent. It is not unpleasand, and resembles benzene to some extent.

The observed boiling points at various pressures are recorded below.

| Pressure | Temperature |
|---|---|
| 18-20 mm. | 98-101° |
| 33 | 116 |
| 38 | 119 |
| 67 | 143-6 |
| 200 | 159 |

It melts at 30.5-30.7°. It is soluble in ether and alcohol, but insoluble in water. On exposure to the air it is immediately oxidized to the yellow arseno compound with the evolution of heat.

Analysis of the arsine was carried out as follows:
Small bulbs resembling Victor Meyer bulbs were blown on long, thin capillaries. The bulb was weighed, heated in a flame, and the tip quickly dropped into the molten arsine. On cooling, a drop of the arsine sucked back into the bulb. This was carefully heated to boiling and the bulb again cooled. The bulb now filled with the arsine. The capillary was drawn rapidly through a flame to expell the arsine in it, and the tip sealed off. It was then weighed. For the determination of arsenic the capillary was broken off and the broken peices together with the bulb wrapped up in a peice of filter paper, the bulb smashed with a hammer, and the package dropped into a 500 cc. Kjeldahl. The proceedure from here on was simply the method of Ewins, the addition of starch being omitted. Chlorine was determined by the method of Carius. The bulb was placed in the digestion tube and broken by dropping in a heavy glass slug. The arsine was then

allowed to oxidize in the air, and the nitric acid added very carefully a drop at a time and with careful cooling, since nitric acid sometimes reacts with explosive with the arseno compound. After the tube was opened, the silver chloride was dissolved out with ammonia, filtered from the glass, and reprecipitated with $HNO_3$. It was, of course, necessary to digest the reprecipitated AgCl for several hours in the dark to obtain a filterable precipitate. Some of the silver chloride usually remained stuck in the peices of capillary and did not dissolve in ammonia. It was necessary to shake the tube until these capillaries were completely broken up against the glass slug.

| | | | | |
|---|---|---|---|---|
| .5147 g. | sample required | 103.64 cc. | $I_2$ sol. | 39.75% As |
| .3622 g. | | 72.20 cc. | | 39.37 |
| 1 cc. $I_2$ sol. = .001975 g. As | | | Average | 39.51 |

| | | | | |
|---|---|---|---|---|
| .4259 g. | sample gave | .3184 g. AgCl | | 18.50% Cl |
| .4592 g. | | .3520 g. | | 18.97 |
| .2539 | | .1914 | | 18.65 |
| | | | Average | 18.71 |

Calculated for $C_6H_4AsCl$: Cl, 18.81%; As, 39.79%

3. p-chlorophenylarsine benzaldehyde condensation product; analysis.

The preparation of this compound and its properties is described in the descriptive part of this paper.

Analytical data:

.1406 g. sample gave .0473 g. AgCl = 8.32% Cl
.1676 g. .0558 g. = 8.23%

.1082 g. required 8.95 cc. $I_2$ sol. 16.34%
.1144 g. required 9.21 cc. $I_2$ sol. 15.90%
1 cc. $I_2$ sol = .001975 g. As
Calculated for $C_2OH_{18}O_2ClAs$: As, 18.63%; Cl, 8.74%

4. p-chlorophenylarsine paraddehyde condensation product; Analysis.

The preparation and properties of this compound are described in the descriptive part of this paper.

Analytical data:

| | | | | |
|---|---|---|---|---|
| .3215 g. | sample gave | .1620 g. AgCl | = | 12.47% Cl |
| .3601 g. | | .1820 g. | = | 12.50% |
| | | Average | | 12.49% |

| | | | |
|---|---|---|---|
| .3674 g. | sample required | 50.01 cc. $I_2$ sol. | 26.88% As |
| .3771 g. | | 52.18 cc. | 27.33% |
| 1 cc $I_2$ sol = .001975 g. As | | Average | 27.11% |

Calculated for $C_{10}$H14 $O_2$ As Cl: Cl, 12.82%; As, 27.12%.

5. Preparation of arsanilic acid and its reduction: Arsanilic acid was first prepared by Bechamp in 1863[24] by heating aniline arsenate to 190-200°. This method is apparently the only one which has been used in preparing this important arsonic acid. The latest modification of this method is that of Cheetham and Schmidt[25], who claim 20% yields when working with small quantities. The modified Bart's reaction had been found in this laboratory to work so smoothly in the preparation of many arsonic acids that it was thought worth while to work out the conditions for the preparation of p-acetylarsanilic acid by this reaction and for its subsequent hydrolysis to arsanilic acid. The preparation of acetylarsanilic acid by Bart's reaction is described in D. R. P. 250,264[26]. The proceedure used in the present investigations was as follows:

50 g. of pure (Eastman) p-aminoacetanilide in 200 cc. $H_2O$ and 100 cc. HCl (s.g. 1.19) was diazotized with 23 g. of solution of $NaNO_2$ in 500 cc. $H_2O$. 120 g. $As_2O_3$ and 200 g. $Na_2CO_3$ were dissolved in 350 cc. $H_2O$ with heating, filtered, and to the filtrate 3 g. $CuSO_4$ was added. To this cooled solution the diazo solution was added with stirring, the mixture made acid with acetic acid, filtered, and the filtrate treated with an excess of HCl. 65 g. of p-acetylaminoarsonic acid was obtained---75% of theory. HCl, NaOH, and $H_2SO_4$ in various concentrations were tried as hydrolytic agents. NaOH was found to give the best results and to permit the isolation of the arsanilic acid most readily. The proceedure was as follows:

[24] Compt. rend. 56, I, 1172 (1863) Abs. in Jahrsbericht (L. & K.) (1863) 414.

[25] J. Am. Chem. Soc. 42, 828, (1920)

[26] Friedlander VIII, 1225

6.5 g. p-acetylaminoarsonic acid was boiled under reflux for 2 hours with 35 cc. of 20% NaOH solution. The mixture was then boiled ten minutes with a little animal charcoal, and filtered into 50 cc. of 95% ethyl alcohol. The resulting solution was cooled with ice and 10 cc. of 40% acetic acid added. Crystals separated out after a short time until the mass was nearly solid. 30 cc more of alcohol was then added and the mixture allowed to stand over night. The sodium salt was then filtered off, and washed with alcohol and ether. Yield, 3.6 g. or 60% of theory. With a little experimentation the yields of this product (calculated on the acetylarsanilic acid) should undoubtedly be run up to very nearly 100%. The amount of sodium hydroxide solution used in this experiment was probably excessive. Using smaller relative amounts of sodium hydroxide solution and working with larger quantities this would undoubtedly be an entirely practicable method for the preparation of arsanilic acid. The process would also be much simplified if the free acid were precipitated out by properly adjusting the hydrogen ion concentration instead of isolating the sodium salt with alcohol.[27] In the hydrolysis it is quite essential that the acid or alkaline hydrolytic agent be not too dilute, since arsanilic acid is decomposed by hot water rather rapidly. In the presence of fairly concentrated acids or alkalies, it is, however, perfectly stable.[28]

Reduction of arsanilic acid: This reduction was carried out precisely as in the case of p-chlorophenylarsonic acid, the proportions being the same. It was, of course, necessary to make the reaction mixture alkaline before steam distilling. It distills much more slowly than does the chlorophenylarsine. The yield of twice redistilled product from 100 g. of arsanilic acid was 24 g.

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27 Sec J. Am. Chem. Soc. 42, 828, (1920)
28 E. Schmitz, Ber., (1914) 47, 363; ibid 996

The product was a colorless liquid boiling at 145-7° under a pressure of 41 mm. This agrees with the description of p-aminophenylarsine in D. R. P. 251, 571.[29]

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[29] Friedlander, XI, 1024.

6. Preparation of p-phenolarsonic acid and its reduction: The method used was that of Jacobs and Heidelberger[30]. Yields of crude product were approximately 20%, but considerably less than this when calculated against the recrystallized product. Contrary to the statements of Jacobs and Heidelberger, tar was always formed, and the crude sodium salt was always colored. This color was removed by a single precipitation from a concentrated aqueous solution by alcohol.

Syrupy arsenic acid was prepared from crude arsenic trioxide according to the method of Vannino (31 ). In dealing with quantities of over 100 g. it is quite important to carry the reaction out in a large dish (not in a flask, or as Vannino recommends, in a retort) and to add the $As_2O_3$ to the acid.

The method used by Jacobs and Heidelberger in isolating the product is very tedious and attempts were made to simplify it. The magnesium salt was isolated in two runs instead of the sodium salt. This was carried out as follows:

The reaction was run as usual, using 450 g. arsenic acid and 200 g. phenol, heating at 150° for 6 hours, and extracting the product with two liter of $H_2O$. This filtered extract was divided into two equal fractions. The sodium salt was isolated from the first by neutralizing with $Ba(OH)_2$, exactly removing the excess barium ions with $H_2SO_4$, filtering, evaporating in vacuo, exactly neutralizing with NaOH, evaporating in vacuo until crystallization began, adding a large excess of alcohol, cooling for 12 hours, and filtering off the sodium salt. The second fraction was treated as follows: 250 g. ice, 300 g. $MgCl_2$, 200 g. $NH_4Cl$, and 100 cc. excess conc. $NH_4OH$, and were added and the mixture allowed to stand for several hours.

30 J. Am. Chem. Soc. (1914) 41, 1446.
31 Handbuck der Prapärativen Chemie I, 184

It was then filtered. The filtrate was heated to boiling, whereupon the magnesium salt of the p-phenolarsonic acid separated. A comparison of the yields from the two fractions is shown below:

| | Run III | Run IV |
|---|---|---|
| Mg salt | 30 g. | 49 g. |
| Na salt | 62 g. | 57 g. |

The isolation of the magnesium salt is extremely simple compared with the isolation of the sodium salt, but the magnesium salt is not so clean a product and the yields are not so good. It is probable that further experimentation would improve both factors and make this process entirely practicable.

The effect of the use of an excess of phenol, instead of an excess of the arsenic acid was tried in one experiment. The excess phenol was removed by distillation in vacuo. A dirty gum was formed from which no crystalline product could be isolated.

Preparation of p-hydroxyphenylarsine: p-phenolarsonic acid was reduced by the same method used in preparing p-chlorophenylarsonic acid excepting that the methyl alcohol was omitted, p-phenolarsonic acid being extremely soluble in water. The reaction mixture was steam distilled. The distillate contained only water. The contents of the reduction flask were then extracted with ether. The extract was black, the black material supposedly coming from the zinc. It was extracted with 10% NaOH. The NaOH extract was black. It was saturated with $CO_2$, and extracted with ether. The ethereal solution was now colorless. It was again extracted with 10% NaOH and the extract saturated with $CO_2$. A buff colored precipitate was formed, apparently the p-dihydroxyarsenobenzene. If HCl was used instead of $CO_2$ as a precipitant, the precipitate was red. All the reactions were carried out in an atmosphere of $CO_2$. p-hydroxyphenylarsine is

described in D. R. P. 251, 571[32] as a white powder which readily decomposes on heating or exposure to the air. Apparently it was not formed in the present case; or else decomposed during the attempt to isolate it.

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[32] Friedlander XI, 1042.

7. Preparation of p-phenetylarsonic acid and its reduction: This acid was prepared in excellent yields from p-phenetidine by the modified Bart's reaction[33]. It was reduced in the same way as the other arsonic acids described above, and the arsine isolated in the same way. The properties of the arsine are described in the descriptive part of this paper.

[33] This preparation was carried out by Mr. G. H. Cheney of this laboratory.

## IV. SUMMARY.

1. The preparation of p-chlorophenylarsine, p-aminophenylarsine, and p-phenetylarsine is described. Of these p-chlorophenyl- and p-phenetyl-arsine are new.

2. The reactions of these arsines with certain aldehydes have been studied.

3. The preparation of p-chlorophenylarsonic acid and of arsanilic acid by the modified Bart's reaction is described.

## V. ACKNOWLEDGEMENT.

This problem was suggested by Professor Roger Adams and the experimental work was done under his direction. The writer expresses his appreciation of the kindly interest and guidance which Professor Adams offered, and without which this investigation would have been impossible.